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10/576,342	12/28/2006	Cyril Delattre	10404.038.00	2294

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EXAMINER	
LAM, ANN Y	
ART UNIT	PAPER NUMBER
1641	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,342	DELATTRE ET AL.	
	Examiner	Art Unit	
	ANN Y. LAM	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☒ Claim(s) *30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/30/08, 12/28/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brennan 5,474,796.

As to claim 1, Brennan discloses that an important characteristic of masked surfaces in patterned oligonucleotide synthesis is that the surface must be poorly wet by common organic solvents such as acetonitrile and the glycol ethers, relative to the more polar fuctionalized binding sites. See column 4, lines 43-50.

It is disclosed that the wetting phenomenon is a measure of the surface tension or attractive forces between molecules at a solid-liquid interface, and is defined in dynes/cm.sup.2. Fluorocarbons have very low surface tension because of the unique polarity (electronegativity) of the carbon-flourine bond. When fluorocarbons are covalently attached to an underlying derivatized solid (highly crosslinked polymeric) support, the density of reactive sites will generally be lower than Langmuir-Blodgett and group density. However, the use of perfluoroalkyl masking agents preserves a

relatively high fluorine content in the solvent accessible region of the supporting surface. See column 4, line 5 to col. 5, line 10.

It is further disclosed by Brennan that the optical properties of glass (polytetrasiloxane) are unsurpassed for detection purposes. There are numerous techniques developed by the semiconductor industry using thick films (1-5 microns) of photoresists to generate masked patterns of exposed glass surfaces. The best method to derivatize the first exposed glass surface is with volatile fluoroalkyl silanes using gas phase diffusion to create closely packed lipophobic monolayers. The polymerized photoresist provides an effectively impermeable barrier to the gaseous fluoroalkyl silane during the time period of derivatization of the exposed region. Following lipophobic derivatization however, the remaining photoresist can be readily removed by dissolution in warm organic solvents to expose a second surface of raw glass, while leaving the first applied silane layer intact. This second region glass can then be derivatized by either solution or gas phase methods with a second, polar silane which contains either a hydroxyl or amino group suitable for anchoring solid phase oligonucleotide synthesis. See column 5, lines 11-30.

Figure 3 depicts the deposition of the reactant solution on a functionalized binding site and subsequent reaction with the surface. A micro-droplet of solution (FIG. 3(a)) is deposited on the functionalized binding site (center cross-hatched region in FIG. 3(b)). Because of the differences in wetting properties of the reactant solution on the functionalized binding site and the surrounding surface, the micro-droplet of the

reactant solution beads on the functionalized binding site and the reactants in solution react with the surface (FIG. 3(c)). (col. 6, lines 8-17)

In an exemplary embodiment, Brennan discloses that a hybridization array is synthesized on a glass plate. The plate is first coated with the stable fluorosiloxane. A CO.sub.2 laser is used to ablate off regions of the fluorosiloxane and expose the underlying silicon dioxide glass. The plate is then coated with glycidyloxypropyl trimethoxysilane, which reacts only on the exposed regions of the glass to form a glycidyl epoxide. The plate is next treated with hexaethyleneglycol and sulfuric acid to convert the glycidyl epoxide into a hydroxyalkyl group, which acts as a linker arm. The hydroxyalkyl group resembles the 5'-hydroxide of nucleotides and provides a stable anchor on which to initiate solid phase synthesis. See column 7, lines 19-40.

Brennan further disclose that the hydroxyalkylsiloxane surface in the dots has a surface tension of approximately .gamma.=47, whereas the fluoroxysilane has a surface tension of .gamma.=18. For oligonucleotide assembly, the solvents of choice are acetonitrile, which has a surface tension of .gamma.=29, and diethylglycol dimethyl ether. The hydroxyalkylsiloxane surface is thus completely wet by acetonitrile, while the fluorosiloxane masked surface between the dots is very poorly wet by acetonitrile. Droplets of oligonucleotide synthesis reagents in acetonitrile are applied to the dot surfaces and tend to bead up, as shown in FIG. 3. Mixing between adjacent dots is prevented by the very hydrophobic barrier of the mask. The plate effectively acts as an array microliter dish, wherein the individual wells are defined by surface tension rather than gravity. See column 7 lines 45-67.

With respect to claim 1, the patterned hydroxylalkylsiloxane that is completely wet by acetonitrile is equivalent to Applicant's uptake areas suitable for taking up a drop of the liquid of interest (acetonitrile with oligonucleotides). The patterned fluorocarbon that is poorly wet by acetonitrile is equivalent to Applicant's claimed non-wetting surfaces. However, the technique of distributing the drops of acetonitrile with oligonucleotides is different from that claimed by Applicant. Brennan disclose using a picopump to apply the nucleotide in acetonitrile, whereas Applicant recites introduction of a liquid of interest into a box enclosing the active surface of a substrate, and extraction of the liquid of interest from the box wherein the surfaces inside the box are substantially non-wetting with respect to the liquid of interest [oligonucleotides in acetonitrile]. Applicant further recites that when extracting the liquid of interest from the box, a drop of liquid of interest remains captive in a distributed and localized manner on each uptake area. While Brennan disclose use of a picopump, for the apparent reason that it can precisely apply liquid reagent where intended and eventually form the array of oligonucleotides, it is understood by the skilled artisan that other methods of applying the oligonucleotide in acetonitrile can be used. The skilled artisan would recognize that such methods include introduction of the oligonucleotide/acetonitrile on the glass substrate covering the hydroalkylsiloxane areas [uptake areas], and then extraction of the liquid of interest, since it is disclosed by Brennan that the fluorosiloxane is hydrophobic [non-wetting] whereas the hydroalkylsiloxane surface areas are completely wet by acetonitrle/oligonucleotides [uptake areas] and thus the oligonucleotides/acetonitrile will remain only in the uptake areas. In other words, the

skilled artisan would have recognized that either method of applying the acetonitrile/oligonucleotides will result in the oligonucleotides being captured in the hydroalkylsiloxane surface areas only and not the hydrophobic fluorosiloxane areas once the excess acetonitrile/oligonucleotides are removed/extracted from the surface. As to providing the surface in a box, it is well within the skills of the ordinary artisan to recognize the simple concept of using such a box to contain excess reagents during introduction of materials.

As to claim 2, assembly of oligonucleotides on the prepared dots (FIG. 2B, bottom) is carried out. Delivery of the appropriate blocked nucleotides and activating agents in acetonitrile is directed to individual dots using the picopump apparatus. Brennan does not disclose means for introducing and extracting liquid of interest in the box since the fluorosiloxane is disclosed as creating a hydrophobic area to prevent cross-contamination or mixing between adjacent dots. Moreover, flooding a surface and then washing the chemicals from the device surface would provide an equivalent means to apply the reagents (oligonucleotides in acetonitrile.)

As to claim 3, the entire glass substrate is equivalent to the claimed working area.

As to claim 4, the uptake area has a ring shape (see e.g., figure 6) and any area within this ring is equivalent to a working area.

As to claim 5, the area for uptake of the oligonucleotides is considered to encircle several working areas, as several portions of the uptake area is considered to be the claimed several working areas.

As to claim 6, the working area is an area for detection of a chemical species (oligonucleotides).

As to claims 7-9, the working area, i.e., where the oligonucleotides are immobilized, is an area functionalized with a biological probe, i.e., the oligonucleotides.

As to claim 10, the working area, [i.e., area functionalized with hydroxyalkylsiloxane, and where the oligonucleotides are eventually immobilized], is an area of chemical interaction with the captive drop [oligonucleotie/acetonitrile].

As to claims 11 and 27, the working area is considered an electrochemical microcell since it is capable of allowing electrochemical interaction and is a small area.

As to claims 12 and 13, the working area is chemical sensor since it comprises oligonucleotides, i.e., chemical actuators, capable of hybridization for detection of complementary oligonucleotides.

As to claim 14, the areas for uptake is a physical uptake area since it physically uptakes the oligonucleotides.

As to claims 15 and 20-21, Brennan does not disclose that the uptake area takes up the drop of liquid of interest via capillary forces. However, Brennan does disclose that mixing between adjacent dots is prevented by the very hydrophobic barrier of the mask. The plate effectively acts as an array microliter dish, wherein the individual wells are defined by surface tension rather than gravity. See column 7 lines 45-67. Thus, providing a physical barrier such that there is capillary forces to also hold the drop of liquid of interest is well within the skills of the ordinary artisan as this is the prior art method of retaining the liquid of interest in a particular desired area.

As to claim 16, the uptake area locally takes up the drop of liquid of interest by wetting (see figure 3 and the discussion above regarding claim 1.)

As to claim 17, the wettability of the hydroxyalkylsiloxane for the acetonitrile/oligonucleotide is greater than the fluorosiloxane [active surface].

As to claim 18, since the uptake is due to wetting, it would have been obvious to the skilled artisan that the uptake may also be by electrowetting which employs similar principles.

As to claim 19, the uptake area takes up the drop of liquid of interest via interactions of hydrophilic/hydrophobic type with the liquid of interest [i.e., via wetting].

As to claims 22 and 23, extraction by suction or injecting a gaseous fluid, would have been obvious to the skilled artisan as suction and removal by injecting a gaseous fluid are well known means to remove liquid material from an area.

As to claim 24, using gaseous fluid that is vapour of the liquid of interest requires only ordinary skills in the art as the skilled artisan as it is predictable that such vapour would remove the fluid from the area.

As to claims 25 and 26, lab-on-chips or biochips are well known in the art as a means to provide a diagnostic assay, and it is predictable that a glass substrate as disclosed by Brennan can be used as a lab-on-chip. Also, the glass substrate with the array of biological materials can itself be considered a lab-on-chip or biochip.

As to claim 28, use of the array on glass substrate for optical detection is disclosed (col. 5, lines 1-10.)

As to claim 29, it is well recognized by the skilled artisan that simultaneous (parallel) detection such as the optical detections disclosed (col. 5, lines 1-10) can be performed.

Allowable Subject Matter

Claim 30 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Examiner, Art Unit 1641